

### **REMARKS**

Claims 33-37, 39, 40 and 52-55 were pending prior to entering the amendments.

#### **The Amendment**

SEQ ID NOs: 1-14 are inserted at the end of the specification. These sequences are identical to those sequences submitted in the paper copy and computer-readable format of the sequence listing on July 18, 2007. Applicants submit that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter (37CFR 1.57(f)).

Claim 33 is amended to recite high grade cervical intraepithelial neoplasia; support for the amendment can be found, for example, page 40, line 5. Claim 33 is also amended to recite that threshold levels of the normalization markers is determined from an adequate and predefined amount of ectocervical cells or endocervical cells; support for the amendment can be found, for example, at page 47, lines 6-19. Claim 33 is further amended to clarify the meaning of the claim. Support for the amendment can be found, for example, at page 47, lines 1-26.

Claim 40 is amended to correct the typographic error of endocervical to ectocervical. Support for the amendment can be found at page 30, lines 5-8 and Table 1.

New Claim 56 is similar to Claim 33 except that it recites determining the presence or absence of a detectable level of at least one normalization marker. Support for the amendment can be found at page 20, lines 24-27.

New Claims 57-62 are similar to Claims 36, 37, 39, 40, 54, and 55.

No new matter is added in any of the amendments. The Examiner is requested to enter the amendment and reconsider the application.

#### **The Response**

##### **Objection to Amendment**

4. Applicants have amended the specification to insert SEQ ID NOs: 1-14. Applicants submit that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter (37CFR 1.57(f)).

### **Objection to the Specification**

5. Applicant have properly identified the trademark of HYBOND®.

### **35 USC §112 Second Paragraph Rejection**

7. Claims 33-37, 39, 40 and 52-55 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner states that it cannot be ascertained how the determination that the sample is adequate, or not, is made by the comparison step; and furthermore, it cannot be ascertained how cervical dysplasia, cervical cancer or cervical intraepithelial neoplasia is detected upon the "basis" of the level of and the adequacy of the sample.

Applicants have amended Claim 33 to recite that threshold levels of the normalization markers is determined from an adequate and predefined amount of ectocervical cells or endocervical cells. At page 47 at lines 9-17, the application describes how to determine a threshold value by measuring the OD value of an adequate and predefined amount of endocervical cells or ectocervical cells. Although the application exemplifies 200,000 squamous ectocervical cells, 2000 columnar endocervical cells and the OD values, it must be understood that the value for the cells as well for OD may vary depending to the reaction conditions. Those of skill in the art know how an appropriate threshold value for a particular test format may be established.

Therefore, the §112 second paragraph rejection should be withdrawn in view of the claim amendment.

### **35 USC §112 First Paragraph Rejection**

9. Claims 33-37, 39, 40 and 52-55 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

The Examiner states that none of the claims are directed to both a particularly identified "relevant marker" and a particularly identified "normalization marker".

Applicants have amended Claim 33 to identify the relevant marker as p16<sup>INK4a</sup> and the normalization markers as proteins having SEQ ID NOs:1-12.

10. Claims 33-37, 39, 40 and 52-55 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for using a process for diagnosing cervical dysplasia or cervical cancer, said process comprising detecting the level of expression p16<sup>INK4a</sup>, does not allegedly provide enablement for using a process for diagnosing any type of cervical intraepithelial neoplasia.

Applicants have amended Claim 33 to recite detecting high grade cervical intraepithelial neoplasia.

The Examiner states that a marker that does not distinguish cervical dysplasia, cervical cancer, and cervical intraepithelial neoplasia cannot be expected to be useful in the differential diagnosis of such conditions or diseases.

Applicants respectfully submit that the claims are directed to a method for detecting cervical dysplasia, cervical cancer, or high grade cervical intraepithelial neoplasia, which is a screening method, and is not a method for differential diagnosis.

The Examiner states that the values of the "threshold levels" of the normalization markers to which the claims refer are not known or disclosed.

Applicants have amended the claim to recite how to determine the threshold levels.

### **35 USC §112 Second Paragraph Rejection**

11. Claims 33-37, 39, 40 and 52-55 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants have amended the claims to address the issues.

### **35 USC §112 First Paragraph Rejection**

Claims 33-37, 39, 40 and 52-55 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

Gamma-Catenin, Ep-Cam, E-Cadherin, alpha-1 Catenin, alpha-2 Catenin, beta-Catenin, Involucrin, and p120 are identified in Table 1 by accession numbers. Cytokeratin 8, 18, 10, and 13, p16<sup>INK4a</sup> and p14ARF are known proteins with well-established sequences. Those skilled in the art would know the exact sequence cytokeatin 8, 18, 10, and 13, p16<sup>INK4a</sup> and p14ARF. In the Response submitted on July 18, 2007, Applicants have already provided NCBI sequences of the above proteins; each sequence is identified by its name and accession number.

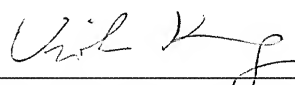
Applicants have amended the specification to insert SEQ ID NOs: 1-14. Applicants submit that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter (37CFR 1.57(f)).

### **Conclusion**

For all the foregoing reasons, reconsideration of and withdrawal of all outstanding rejections is respectfully requested. The Examiner is earnestly solicited to allow all claims, and pass this application to issuance.

Respectfully submitted,

Date: October 30, 2007

  
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Viola T. Kung, Ph.D. (Reg. No. 41,131)

Enclose: Paper copy of Sequence Listing

HOWREY LLP  
2941 Fairview Park Drive, **Box No. 7**  
Falls Church, VA 22042  
Telephone No. (650) 798-3570  
Facsimile No. (650) 798-3600

# SEQUENCE LISTING

<110> Rudiger Ridder, et.al.  
 <120> Method for solution based diagnosis  
 <130> 05033.0003.00US00  
 <140> 10/633,484  
 <141> 2003-07-31  
 <150> EP 02017313.4  
 <151> 2002-08-01  
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Cys Gly Arg Gln Tyr Thr Leu Lys Lys Thr Thr Thr Tyr Thr Gln Gly  
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Val Pro Pro Ser Gln Gly Asp Leu Glu Tyr Gln Met Ser Thr Thr Ala  
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Arg Ala Lys Arg Val Arg Glu Ala Met Cys Ser Gly Val Ser Gly Glu  
 85 90 95

Asp Ser Ser Leu Leu Leu Ala Thr Gln Val Glu Gly Gln Ala Thr Asn  
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Leu Gln Arg Leu Ala Glu Pro Ser Gln Leu Leu Lys Ser Ala Ile Val  
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His Leu Ile Asn Tyr Gln Asp Asp Ala Glu Leu Ala Thr Arg Ala Leu  
 Page 1

130

135

140

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Ser Gly Gly Ile Pro Ala Leu Val Arg Met Leu Ser Ser Pro Val Glu  
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Thr Asp Cys Leu Gln Leu Leu Ala Tyr Gly Asn Gln Glu Ser Lys Leu  
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Ile Ile Leu Ala Asn Gly Gly Pro Gln Ala Leu Val Gln Ile Met Arg  
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Val Gln Asn Cys Leu Trp Thr Leu Arg Asn Leu Ser Asp Val Ala Thr  
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Lys Gln Glu Gly Leu Glu Ser Val Leu Lys Ile Leu Val Asn Gln Leu  
 Page 2

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 Ser Val Asp Asp Val Asn Val Leu Thr Cys Ala Thr Gly Thr Leu Ser  
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 Asp Asp Ile Thr Glu Pro Ala Val Cys Ala Leu Arg His Leu Thr Ser  
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Page 7

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Pro Asp Thr Phe Met Glu Gln Lys Ile Thr Tyr Arg Ile Trp Arg Asp  
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Thr Ala Asn Trp Leu Glu Ile Asn Pro Asp Thr Gly Ala Ile Ser Thr  
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Arg Ala Glu Leu Asp Arg Glu Asp Phe Glu His Val Lys Asn Ser Thr  
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 Tyr Lys Ala Leu Lys Pro Glu Val Asp Lys Leu Asn Ile Met Ala Ala  
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 Lys Arg Gln Gln Glu Leu Lys Asp Val Gly His Arg Asp Gln Met Ala  
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 Ala Ala Arg Gly Ile Leu Gln Lys Asn Val Pro Ile Leu Tyr Thr Ala  
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 Ser Gln Ala Cys Leu Gln His Pro Asp Val Ala Ala Tyr Lys Ala Asn  
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 820 825 830



Val Lys Ala Ser Tyr Val Ala Ser Thr Lys Tyr Gln Lys Ser Gln Gly  
835 840 845

Met Ala Ser Leu Asn Leu Pro Ala Val Ser Trp Lys Met Lys Ala Pro  
850 855 860

Glu Lys Lys Pro Leu Val Lys Arg Glu Lys Gln Asp Glu Thr Gln Thr  
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Lys Lys Lys Gly Arg Ser Lys Lys Ala His Val Leu Ala Ala Ser Val  
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Glu Gln Ala Thr Gln Asn Phe Leu Glu Lys Gly Glu Gln Ile Ala Lys  
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Glu Ser Gln Asp Leu Lys Glu Glu Leu Val Ala Ala Val Glu Asp Val  
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Arg Lys Gln Gly Glu Thr Met Arg Ile Ala Ser Ser Glu Phe Ala Asp  
100 105 110

Asp Pro Cys Ser Ser Val Lys Arg Gly Thr Met Val Arg Ala Ala Arg  
Page 13

115

120

125

Ala Leu Leu Ser Ala Val Thr Arg Leu Leu Ile Leu Ala Asp Met Ala  
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Arg Gln Gln Glu Leu Lys Asp Pro His Cys Arg Asp Glu Met Ala Ala  
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Ala Arg Gly Ala Leu Lys Lys Asn Ala Thr Met Leu Tyr Thr Ala Ser  
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Gln Ala Phe Leu Arg His Pro Asp Val Ala Ala Thr Arg Ala Asn Arg  
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Asp Tyr Val Phe Lys Gln Val Gln Glu Ala Ile Ala Gly Ile Ser Asn  
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Ala Ala Gln Ala Thr Ser Pro Thr Asp Glu Ala Lys Gly His Thr Gly  
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Ile Gly Glu Leu Ala Ala Ala Leu Asn Glu Phe Asp Asn Lys Ile Ile  
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Leu Asp Pro Met Thr Phe Ser Glu Ala Arg Phe Arg Pro Ser Leu Glu  
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Glu Arg Leu Glu Ser Ile Ile Ser Gly Ala Ala Leu Met Ala Asp Ser  
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Ser Cys Thr Arg Asp Asp Arg Arg Glu Arg Ile Val Ala Glu Cys Asn  
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 Page 14

370

375

380

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Val Leu Ile Glu Ala Ala Lys Ser Gly Asn Glu Lys Glu Val Lys Glu  
 405 410 415

Tyr Ala Gln Val Phe Arg Glu His Ala Asn Lys Leu Val Glu Val Ala  
 420 425 430

Asn Leu Ala Cys Ser Ile Ser Asn Asn Glu Glu Gly Val Lys Leu Val  
 435 440 445

Arg Met Ala Ala Thr Gln Ile Asp Ser Leu Cys Pro Gln Val Ile Asn  
 450 455 460

Ala Ala Leu Thr Leu Ala Ala Arg Pro Gln Ser Lys Val Ala Gln Asp  
 465 470 475 480

Asn Met Asp Val Phe Lys Asp Gln Trp Glu Lys Gln Val Arg Val Leu  
 485 490 495

Thr Glu Ala Val Asp Asp Ile Thr Ser Val Asp Asp Phe Leu Ser Val  
 500 505 510

Ser Glu Asn His Ile Leu Glu Asp Val Asn Lys Cys Val Ile Ala Leu  
 515 520 525

Gln Glu Gly Asp Val Asp Thr Leu Asp Arg Thr Ala Gly Ala Ile Arg  
 530 535 540

Gly Arg Ala Ala Arg Val Ile His Ile Ile Asn Ala Glu Met Glu Asn  
 545 550 555 560

Tyr Glu Ala Gly Val Tyr Thr Glu Lys Val Leu Glu Ala Thr Lys Leu  
 565 570 575

Leu Ser Glu Thr Val Met Pro Arg Phe Ala Glu Gln Val Glu Val Ala  
 580 585 590

Ile Glu Ala Leu Ser Ala Asn Val Pro Gln Pro Phe Glu Glu Asn Glu  
 595 600 605

Phe Ile Asp Ala Ser Arg Leu Val Tyr Asp Gly Val Arg Asp Ile Arg  
 610 615 620

Lys Ala Val Leu Met Ile Arg Thr Pro Glu Glu Leu Glu Asp Asp Ser  
 Page 15

625		630		635		640
Asp Phe Glu Gln	Glu 645	Asp Tyr Asp Val	Arg 650	Ser Arg Thr Ser	Val 655	Gln
Thr Glu Asp	Asp 660	Gln Leu Ile Ala	Gly 665	Gln Ser Ala Arg	Ala 670	Ile Met
Ala Gln Leu	Pro 675	Gln Glu Glu	Lys 680	Ala Lys Ile Ala	Glu 685	Gln Val Glu
Ile Phe His	Gln Glu Lys	Ser 695	Lys Leu Asp	Ala 700	Glu Val Ala	Lys Trp
Asp 705	Asp Ser Gly	Asn 710	Ile Ile Val	Leu Ala 715	Lys Gln Met	Cys Met 720
Ile Met Met	Glu 725	Met Thr Asp	Phe Thr Arg 730	Gly Lys Gly	Pro Leu 735	Lys
Asn Thr Ser	Asp 740	Val Ile Asn	Ala 745	Lys Lys Ile Ala	Glu 750	Ala Gly
Ser Arg	Met 755	Asp Lys Leu	Ala Arg 760	Ala Val Ala	Asp Gln 765	Cys Pro Asp
Ser Ala	Cys 770	Lys Gln Asp	Leu 775	Leu Ala Tyr	Leu Gln 780	Arg Ile Ala Leu
Tyr 785	Cys His Gln	Leu 790	Asn Ile Cys	Ser Lys Val 795	Lys Ala Glu	Val Gln 800
Asn Leu Gly	Gly 805	Glu Leu Ile	Val Ser Gly 810	Thr Gly Val	Gln Ser 815	Thr
Phe Thr Thr	Phe 820	Tyr Glu Val	Asp Cys 825	Asp Val Ile	Asp Gly 830	Gly Arg
Ala Ser	Gln 835	Leu Ser Thr	His Leu 840	Pro Thr Cys	Ala Glu 845	Gly Ala Pro
Ile Gly	Ser 850	Gly Ser Ser	Asp 855	Ser Ser Met	Leu Asp 860	Ser Ala Thr Ser
Leu 865	Ile Gln Ala	Ala Lys 870	Asn Leu Met	Asn Ala 875	Val Val Leu	Thr Val 880
Lys Ala Ser	Tyr Val	Ala Ser Thr	Lys Tyr Gln	Lys Val Tyr	Gly Thr	

885                      890                      895  
 Ala Ala Val Asn Ser Pro Val Val Ser Trp Lys Met Lys Ala Pro Glu  
                     900                      905                      910  
 Lys Lys Pro Leu Val Lys Arg Glu Lys Pro Glu Glu Phe Gln Thr Arg  
                     915                      920                      925  
 Val Arg Arg Gly Ser Gln Lys Lys His Ile Ser Pro Val Gln Ala Leu  
                     930                      935                      940  
 Ser Glu Phe Lys Ala Met Asp Ser Phe  
 945                      950

<210> 6  
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 <213> Homo sapiens

<220>  
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 <222> (1)..(781)  
 <223> beta-Catenin, Swissprot Accession P35222

<400> 6

Met Ala Thr Gln Ala Asp Leu Met Glu Leu Asp Met Ala Met Glu Pro  
 1                      5                      10                      15  
 Asp Arg Lys Ala Ala Val Ser His Trp Gln Gln Gln Ser Tyr Leu Asp  
                     20                      25                      30  
 Ser Gly Ile His Ser Gly Ala Thr Thr Thr Ala Pro Ser Leu Ser Gly  
                     35                      40                      45  
 Lys Gly Asn Pro Glu Glu Glu Asp Val Asp Thr Ser Gln Val Leu Tyr  
                     50                      55                      60  
 Glu Trp Glu Gln Gly Phe Ser Gln Ser Phe Thr Gln Glu Gln Val Ala  
 65                      70                      75                      80  
 Asp Ile Asp Gly Gln Tyr Ala Met Thr Arg Ala Gln Arg Val Arg Ala  
                     85                      90                      95  
 Ala Met Phe Pro Glu Thr Leu Asp Glu Gly Met Gln Ile Pro Ser Thr  
                     100                      105                      110  
 Gln Phe Asp Ala Ala His Pro Thr Asn Val Gln Arg Leu Ala Glu Pro  
                     115                      120                      125

Ser Gln Met Leu Lys His Ala Val Val Asn Leu Ile Asn Tyr Gln Asp  
 130 135 140  
 Asp Ala Glu Leu Ala Thr Arg Ala Ile Pro Glu Leu Thr Lys Leu Leu  
 145 150 155 160  
 Asn Asp Glu Asp Gln Val Val Val Asn Lys Ala Ala Val Met Val His  
 165 170 175  
 Gln Leu Ser Lys Lys Glu Ala Ser Arg His Ala Ile Met Arg Ser Pro  
 180 185 190  
 Gln Met Val Ser Ala Ile Val Arg Thr Met Gln Asn Thr Asn Asp Val  
 195 200 205  
 Glu Thr Ala Arg Cys Thr Ala Gly Thr Leu His Asn Leu Ser His His  
 210 215 220  
 Arg Glu Gly Leu Leu Ala Ile Phe Lys Ser Gly Gly Ile Pro Ala Leu  
 225 230 235 240  
 Val Lys Met Leu Gly Ser Pro Val Asp Ser Val Leu Phe Tyr Ala Ile  
 245 250 255  
 Thr Thr Leu His Asn Leu Leu Leu His Gln Glu Gly Ala Lys Met Ala  
 260 265 270  
 Val Arg Leu Ala Gly Gly Leu Gln Lys Met Val Ala Leu Leu Asn Lys  
 275 280 285  
 Thr Asn Val Lys Phe Leu Ala Ile Thr Thr Asp Cys Leu Gln Ile Leu  
 290 295 300  
 Ala Tyr Gly Asn Gln Glu Ser Lys Leu Ile Ile Leu Ala Ser Gly Gly  
 305 310 315 320  
 Pro Gln Ala Leu Val Asn Ile Met Arg Thr Tyr Thr Tyr Glu Lys Leu  
 325 330 335  
 Leu Trp Thr Thr Ser Arg Val Leu Lys Val Leu Ser Val Cys Ser Ser  
 340 345 350  
 Asn Lys Pro Ala Ile Val Glu Ala Gly Gly Met Gln Ala Leu Gly Leu  
 355 360 365  
 His Leu Thr Asp Pro Ser Gln Arg Leu Val Gln Asn Cys Leu Trp Thr  
 370 375 380

Leu Arg Asn Leu Ser Asp Ala Ala Thr Lys Gln Glu Gly Met Glu Gly  
 385 390 400  
 Leu Leu Gly Thr Leu Val Gln Leu Leu Gly Ser Asp Asp Ile Asn Val  
 405 410 415  
 Val Thr Cys Ala Ala Gly Ile Leu Ser Asn Leu Thr Cys Asn Asn Tyr  
 420 425 430  
 Lys Asn Lys Met Met Val Cys Gln Val Gly Gly Ile Glu Ala Leu Val  
 435 440 445  
 Arg Thr Val Leu Arg Ala Gly Asp Arg Glu Asp Ile Thr Glu Pro Ala  
 450 455 460  
 Ile Cys Ala Leu Arg His Leu Thr Ser Arg His Gln Glu Ala Glu Met  
 465 470 475 480  
 Ala Gln Asn Ala Val Arg Leu His Tyr Gly Leu Pro Val Val Val Lys  
 485 490 495  
 Leu Leu His Pro Pro Ser His Trp Pro Leu Ile Lys Ala Thr Val Gly  
 500 505 510  
 Leu Ile Arg Asn Leu Ala Leu Cys Pro Ala Asn His Ala Pro Leu Arg  
 515 520 525  
 Glu Gln Gly Ala Ile Pro Arg Leu Val Gln Leu Leu Val Arg Ala His  
 530 535 540  
 Gln Asp Thr Gln Arg Arg Thr Ser Met Gly Gly Thr Gln Gln Gln Phe  
 545 550 555 560  
 Val Glu Gly Val Arg Met Glu Glu Ile Val Glu Gly Cys Thr Gly Ala  
 565 570 575  
 Leu His Ile Leu Ala Arg Asp Val His Asn Arg Ile Val Ile Arg Gly  
 580 585 590  
 Leu Asn Thr Ile Pro Leu Phe Val Gln Leu Leu Tyr Ser Pro Ile Glu  
 595 600 605  
 Asn Ile Gln Arg Val Ala Ala Gly Val Leu Cys Glu Leu Ala Gln Asp  
 610 615 620  
 Lys Glu Ala Ala Glu Ala Ile Glu Ala Glu Gly Ala Thr Ala Pro Leu  
 625 630 635 640

Thr Glu Leu Leu His Ser Arg Asn Glu Gly Val Ala Thr Tyr Ala Ala  
645 650 655

Ala Val Leu Phe Arg Met Ser Glu Asp Lys Pro Gln Asp Tyr Lys Lys  
660 665 670

Arg Leu Ser Val Glu Leu Thr Ser Ser Leu Phe Arg Thr Glu Pro Met  
675 680 685

Ala Trp Asn Glu Thr Ala Asp Leu Gly Leu Asp Ile Gly Ala Gln Gly  
690 695 700

Glu Pro Leu Gly Tyr Arg Gln Asp Asp Pro Ser Tyr Arg Ser Phe His  
705 710 715 720

Ser Gly Gly Tyr Gly Gln Asp Ala Leu Gly Met Asp Pro Met Met Glu  
725 730 735

His Glu Met Gly Gly His His Pro Gly Ala Asp Tyr Pro Val Asp Gly  
740 745 750

Leu Pro Asp Leu Gly His Ala Gln Asp Leu Met Asp Gly Leu Pro Pro  
755 760 765

Gly Asp Ser Asn Gln Leu Ala Trp Phe Asp Thr Asp Leu  
770 775 780

<210> 7  
<211> 585  
<212> PRT  
<213> Homo sapiens

<220>  
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<222> (1)..(585)  
<223> Involucrin, Swissprot Accession P07476

<400> 7

Met Ser Gln Gln His Thr Leu Pro Val Thr Leu Ser Pro Ala Leu Ser  
1 5 10 15

Gln Glu Leu Leu Lys Thr Val Pro Pro Val Asn Thr His Gln Glu  
20 25 30

Gln Met Lys Gln Pro Thr Pro Leu Pro Pro Pro Cys Gln Lys Val Pro  
35 40 45

Val Glu Leu Pro Val Glu Val Pro Ser Lys Gln Glu Glu Lys His Met  
50 55 60



Thr Ala Val Lys Gly Leu Pro Glu Gln Glu Cys Glu Gln Gln Gln Lys  
 65 70 75 80  
 Glu Pro Gln Glu Gln Glu Leu Gln Gln Gln His Trp Glu Gln His Glu  
 85 90 95  
 Glu Tyr Gln Lys Ala Glu Asn Pro Glu Gln Gln Leu Lys Gln Glu Lys  
 100 105 110  
 Thr Gln Arg Asp Gln Gln Leu Asn Lys Gln Leu Glu Glu Glu Lys Lys  
 115 120 125  
 Leu Leu Asp Gln Gln Leu Asp Gln Glu Leu Val Lys Arg Asp Glu Gln  
 130 135 140  
 Leu Gly Met Lys Lys Glu Gln Leu Leu Glu Leu Pro Glu Gln Gln Glu  
 145 150 155 160  
 Gly His Leu Lys His Leu Glu Gln Gln Glu Gly Gln Leu Lys His Pro  
 165 170 175  
 Glu Gln Gln Glu Gly Gln Leu Glu Leu Pro Glu Gln Gln Glu Gly Gln  
 180 185 190  
 Leu Glu Leu Pro Glu Gln Gln Glu Gly Gln Leu Glu Leu Pro Glu Gln  
 195 200 205  
 Gln Glu Gly Gln Leu Glu Leu Pro Glu Gln Gln Glu Gly Gln Leu Glu  
 210 215 220  
 Leu Pro Gln Gln Gln Glu Gly Gln Leu Glu Leu Ser Glu Gln Gln Glu  
 225 230 235 240  
 Gly Gln Leu Glu Leu Ser Glu Gln Gln Glu Gly Gln Leu Glu Leu Ser  
 245 250 255  
 Glu Gln Gln Glu Gly Gln Leu Lys His Leu Glu His Gln Glu Gly Gln  
 260 265 270  
 Leu Glu Val Pro Glu Glu Gln Met Gly Gln Leu Lys Tyr Leu Glu Gln  
 275 280 285  
 Gln Glu Gly Gln Leu Lys His Leu Asp Gln Gln Glu Lys Gln Pro Glu  
 290 295 300  
 Leu Pro Glu Gln Gln Met Gly Gln Leu Lys His Leu Glu Gln Gln Glu  
 305 310 315 320

Gly Gln Pro Lys His<sub>325</sub> Leu Glu Gln Gln Glu<sub>330</sub> Gly Gln Leu Glu Gln<sub>335</sub> Leu  
 Glu Glu Gln Glu<sub>340</sub> Gly Gln Leu Lys His<sub>345</sub> Leu Glu Gln Gln Glu<sub>350</sub> Gly Gln  
 Leu Glu His<sub>355</sub> Leu Glu His Gln Glu<sub>360</sub> Gly Gln Leu Gly Leu<sub>365</sub> Pro Glu Gln  
 Gln Val<sub>370</sub> Leu Gln Leu Lys Gln<sub>375</sub> Leu Glu Lys Gln Gln<sub>380</sub> Gly Gln Pro Lys  
 His<sub>385</sub> Leu Glu Glu Glu Glu<sub>390</sub> Gly Gln Leu Lys His<sub>395</sub> Leu Val Gln Gln Glu<sub>400</sub>  
 Gly Gln Leu Lys His<sub>405</sub> Leu Val Gln Gln Glu<sub>410</sub> Gly Gln Leu Glu Gln<sub>415</sub> Gln  
 Glu Arg Gln Val<sub>420</sub> Glu His Leu Glu Gln<sub>425</sub> Gln Val Gly Gln Leu<sub>430</sub> Lys His  
 Leu Glu Glu<sub>435</sub> Gln Glu Gly Gln Leu<sub>440</sub> Lys His Leu Glu Gln<sub>445</sub> Gln Gln Gly  
 Gln Leu Glu Val Pro Glu Gln<sub>455</sub> Gln Val Gly Gln Pro<sub>460</sub> Lys Asn Leu Glu  
 Gln Glu Glu Lys Gln Leu<sub>470</sub> Glu Leu Pro Glu Gln<sub>475</sub> Gln Glu Gly Gln Val<sub>480</sub>  
 Lys His Leu Glu Lys<sub>485</sub> Gln Glu Ala Gln Leu<sub>490</sub> Glu Leu Pro Glu Gln<sub>495</sub> Gln  
 Val Gly Gln Pro<sub>500</sub> Lys His Leu Glu Gln<sub>505</sub> Gln Glu Lys His Leu<sub>510</sub> Glu His  
 Pro Glu Gln<sub>515</sub> Gln Asp Gly Gln Leu<sub>520</sub> Lys His Leu Glu Gln<sub>525</sub> Gln Glu Gly  
 Gln Leu<sub>530</sub> Lys Asp Leu Glu Gln<sub>535</sub> Gln Lys Gly Gln Leu<sub>540</sub> Glu Gln Pro Val  
 Phe<sub>545</sub> Ala Pro Ala Pro Gly<sub>550</sub> Gln Val Gln Asp Ile<sub>555</sub> Gln Pro Ala Leu<sub>560</sub> Pro  
 Thr Lys Gly Glu Val<sub>565</sub> Leu Leu Pro Val Glu<sub>570</sub> His Gln Gln Gln Lys<sub>575</sub> Gln

Glu Val Gln Trp Pro Pro Lys His Lys  
580 585

<210> 8  
<211> 483  
<212> PRT  
<213> Homo sapiens

<220>  
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<222> (1)..(483)  
<223> CK8, Swissprot Accession NP\_002264

<400> 8

Met Ser Ile Arg Val Thr Gln Lys Ser Tyr Lys Val Ser Thr Ser Gly  
1 5 10 15

Pro Arg Ala Phe Ser Ser Arg Ser Tyr Thr Ser Gly Pro Gly Ser Arg  
20 25 30

Ile Ser Ser Ser Ser Phe Ser Arg Val Gly Ser Ser Asn Phe Arg Gly  
35 40 45

Gly Leu Gly Gly Gly Tyr Gly Gly Ala Ser Gly Met Gly Gly Ile Thr  
50 55 60

Ala Val Thr Val Asn Gln Ser Leu Leu Ser Pro Leu Val Leu Glu Val  
65 70 75 80

Asp Pro Asn Ile Gln Ala Val Arg Thr Gln Glu Lys Glu Gln Ile Lys  
85 90 95

Thr Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu  
100 105 110

Glu Gln Gln Asn Lys Met Leu Glu Thr Lys Trp Ser Leu Leu Gln Gln  
115 120 125

Gln Lys Thr Ala Arg Ser Asn Met Asp Asn Met Phe Glu Ser Tyr Ile  
130 135 140

Asn Asn Leu Arg Arg Gln Leu Glu Thr Leu Gly Gln Glu Lys Leu Lys  
145 150 155 160

Leu Glu Ala Glu Leu Gly Asn Met Gln Gly Leu Val Glu Asp Phe Lys  
165 170 175

Asn Lys Tyr Glu Asp Glu Ile Asn Lys Arg Thr Glu Met Glu Asn Glu  
180 185 190

Phe Val Leu Ile Lys Lys Asp Val Asp Glu Ala Tyr Met Asn Lys Val  
195 200 205

Glu Leu Glu Ser Arg Leu Glu Gly Leu Thr Asp Glu Ile Asn Phe Leu  
210 215 220

Arg Gln Leu Tyr Glu Glu Glu Ile Arg Glu Leu Gln Ser Gln Ile Ser  
225 230 235 240

Asp Thr Ser Val Val Leu Ser Met Asp Asn Ser Arg Ser Leu Asp Met  
245 250 255

Asp Ser Ile Ile Ala Glu Val Lys Ala Gln Tyr Glu Asp Ile Ala Asn  
260 265 270

Arg Ser Arg Ala Glu Ala Glu Ser Met Tyr Gln Ile Lys Tyr Glu Glu  
275 280 285

Leu Gln Ser Leu Ala Gly Lys His Gly Asp Asp Leu Arg Arg Thr Lys  
290 295 300

Thr Glu Ile Ser Glu Met Asn Arg Asn Ile Ser Arg Leu Gln Ala Glu  
305 310 315 320

Ile Glu Gly Leu Lys Gly Gln Arg Ala Ser Leu Glu Ala Ala Ile Ala  
325 330 335

Asp Ala Glu Gln Arg Gly Glu Leu Ala Ile Lys Asp Ala Asn Ala Lys  
340 345 350

Leu Ser Glu Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met Ala  
355 360 365

Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Asn Val Lys Leu Ala Leu  
370 375 380

Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu Ser  
385 390 395 400

Arg Leu Glu Ser Gly Met Gln Asn Met Ser Ile His Thr Lys Thr Thr  
405 410 415

Ser Gly Tyr Ala Gly Gly Leu Ser Ser Ala Tyr Gly Gly Leu Thr Ser  
420 425 430

Pro Gly Leu Ser Tyr Ser Leu Gly Ser Ser Phe Gly Ser Gly Ala Gly  
435 440 445

Ser Ser Ser Phe Ser Arg Thr Ser Ser Ser Arg Ala Val Val Val Lys  
450 455 460

Lys Ile Glu Thr Arg Asp Gly Lys Leu Val Ser Glu Ser Ser Asp Val  
465 470 475 480

Leu Pro Lys

<210> 9  
<211> 430  
<212> PRT  
<213> Homo sapiens

<220>  
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<222> (1)..(423)  
<223> CK18, Swissprot Accession NP\_954657

<400> 9

Met Ser Phe Thr Thr Arg Ser Thr Phe Ser Thr Asn Tyr Arg Ser Leu  
1 5 10 15

Gly Ser Val Gln Ala Pro Ser Tyr Gly Ala Arg Pro Val Ser Ser Ala  
20 25 30

Ala Ser Val Tyr Ala Gly Ala Gly Gly Ser Gly Ser Arg Ile Ser Val  
35 40 45

Ser Arg Ser Thr Ser Phe Arg Gly Gly Met Gly Ser Gly Gly Leu Ala  
50 55 60

Thr Gly Ile Ala Gly Gly Leu Ala Gly Met Gly Gly Ile Gln Asn Glu  
65 70 75 80

Lys Glu Thr Met Gln Ser Leu Asn Asp Arg Leu Ala Ser Tyr Leu Asp  
85 90 95

Arg Val Arg Ser Leu Glu Thr Glu Asn Arg Arg Leu Glu Ser Lys Ile  
100 105 110

Arg Glu His Leu Glu Lys Lys Gly Pro Gln Val Arg Asp Trp Ser His  
115 120 125

Tyr Phe Lys Ile Ile Glu Asp Leu Arg Ala Gln Ile Phe Ala Asn Thr  
130 135 140

Val Asp Asn Ala Arg Ile Val Leu Gln Ile Asp Asn Ala Arg Leu Ala  
Page 25

145		150		155		160
Ala	Asp	Asp	Phe	Arg 165	Val	Lys
					Tyr	Glu
					Thr	Glu
					Leu	Ala
					Met	Arg
					Gln	
Ser	Val	Glu	Asn 180	Asp	Ile	His
					Gly	Leu
					Arg	Lys
					Val	Ile
					Asp	Asp
					Thr	
Asn	Ile	Thr 195	Arg	Leu	Gln	Leu
					Glu	Thr
					Glu	Ile
					Glu	Ala
					Leu	Lys
					Glu	
Glu	Leu 210	Leu	Phe	Met	Lys	Lys
					Asn	His
					Glu	Glu
					Glu	Val
					Lys	Gly
					Leu	
Gln	Ala	Gln	Ile	Ala	Ser 230	Ser
225					Gly	Leu
					Thr	Val
					Glu	Val
					Asp	Ala
					Pro	
240						
Lys	Ser	Gln	Asp	Leu 245	Ala	Lys
					Ile	Met
					Ala	Asp
					Ile	Arg
					Ala	Gln
					Tyr	
255						
Asp	Glu	Leu	Ala 260	Arg	Lys	Asn
					Arg	Glu
					Glu	Leu
					Asp	Lys
					Tyr	Trp
					Ser	
270						
Gln	Gln	Ile 275	Glu	Glu	Ser	Thr
					Thr	Val
					Val	Val
					Thr	Thr
					Gln	Ser
					Ala	Glu
285						
Val	Gly 290	Ala	Ala	Glu	Thr	Thr
					Leu	Thr
					Glu	Leu
					Arg	Arg
					Thr	Val
					Gln	
300						
Ser	Leu	Glu	Ile	Asp	Leu 310	Asp
305					Ser	Met
					Arg	Asn
					Leu	Lys
					Ala	Ser
					Leu	
320						
Glu	Asn	Ser	Leu	Arg 325	Glu	Val
					Glu	Ala
					Arg	Tyr
					Ala	Leu
					Gln	Met
					Glu	
335						
Gln	Leu	Asn	Gly 340	Ile	Leu	Leu
					His	Leu
					Glu	Ser
					Glu	Leu
					Ala	Gln
					Thr	
345						
Arg	Ala	Glu	Gly	Gln	Arg	Gln
					Ala	Gln
					Glu	Tyr
					Glu	Ala
					Leu	Leu
					Asn	
355						
Ile	Lys 370	Val	Lys	Leu	Glu	Ala
					Glu	Ile
					Ala	Thr
					Tyr	Arg
					Arg	Arg
					Leu	Leu
375						
Glu	Asp	Gly	Glu	Asp	Phe 390	Asn
385					Leu	Gly
					Asp	Ala
					Leu	Asp
					Ser	Ser
					Asn	
400						
Ser	Met	Gln	Thr	Ile	Gln	Lys
					Thr	Thr
					Thr	Arg
					Arg	Ile
					Val	Asp
					Gly	

405 410 415

Lys Val Val Ser Glu Thr Asn Asp Thr Lys Val Leu Arg His  
420 425 430

<210> 10  
<211> 593  
<212> PRT  
<213> Homo sapiens

<220>  
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<222> (1)..(584)  
<223> CK10, Swissprot Accession P13645

<400> 10

Met Ser Val Arg Tyr Ser Ser Ser Lys His Tyr Ser Ser Ser Arg Ser  
1 5 10 15

Gly Gly Gly Gly Gly Gly Gly Gly Cys Gly Gly Gly Gly Gly Val Ser  
20 25 30

Ser Leu Arg Ile Ser Ser Ser Lys Gly Ser Leu Gly Gly Gly Phe Ser  
35 40 45

Ser Gly Gly Phe Ser Gly Gly Ser Phe Ser Arg Gly Ser Ser Gly Gly  
50 55 60

Gly Cys Phe Gly Gly Ser Ser Gly Gly Tyr Gly Gly Leu Gly Gly Phe  
65 70 75 80

Gly Gly Gly Ser Phe Arg Gly Ser Tyr Gly Ser Ser Ser Phe Gly Gly  
85 90 95

Ser Tyr Gly Gly Ser Phe Gly Gly Gly Ser Phe Gly Gly Gly Ser Phe  
100 105 110

Gly Gly Gly Ser Phe Gly Gly Gly Gly Phe Gly Gly Gly Gly Phe Gly  
115 120 125

Gly Gly Phe Gly Gly Gly Phe Gly Gly Asp Gly Gly Leu Leu Ser Gly  
130 135 140

Asn Glu Lys Val Thr Met Gln Asn Leu Asn Asp Arg Leu Ala Ser Tyr  
145 150 155 160

Leu Asp Lys Val Arg Ala Leu Glu Glu Ser Asn Tyr Glu Leu Glu Gly  
165 170 175

Lys Ile Lys Glu Trp Tyr Glu Lys His Gly Asn Ser His Gln Gly Glu  
 180 185 190  
 Pro Arg Asp Tyr Ser Lys Tyr Tyr Lys Thr Ile Asp Asp Leu Lys Asn  
 195 200 205  
 Gln Ile Leu Asn Leu Thr Thr Asp Asn Ala Asn Ile Leu Leu Gln Ile  
 210 215 220  
 Asp Asn Ala Arg Leu Ala Ala Asp Asp Phe Arg Leu Lys Tyr Glu Asn  
 225 230 235 240  
 Glu Val Ala Leu Arg Gln Ser Val Glu Ala Asp Ile Asn Gly Leu Arg  
 245 250 255  
 Arg Val Leu Asp Glu Leu Thr Leu Thr Lys Ala Asp Leu Glu Met Gln  
 260 265 270  
 Ile Glu Ser Leu Thr Glu Glu Leu Ala Tyr Leu Lys Lys Asn His Glu  
 275 280 285  
 Glu Glu Met Lys Asp Leu Arg Asn Val Ser Thr Gly Asp Val Asn Val  
 290 295 300  
 Glu Met Asn Ala Ala Pro Gly Val Asp Leu Thr Gln Leu Leu Asn Asn  
 305 310 315 320  
 Met Arg Ser Gln Tyr Glu Gln Leu Ala Glu Gln Asn Arg Lys Asp Ala  
 325 330 335  
 Glu Ala Trp Phe Asn Glu Lys Ser Lys Glu Leu Thr Thr Glu Ile Asp  
 340 345 350  
 Asn Asn Ile Glu Gln Ile Ser Ser Tyr Lys Ser Glu Ile Thr Glu Leu  
 355 360 365  
 Arg Arg Asn Val Gln Ala Leu Glu Ile Glu Leu Gln Ser Gln Leu Ala  
 370 375 380  
 Leu Lys Gln Ser Leu Glu Ala Ser Leu Ala Glu Thr Glu Gly Arg Tyr  
 385 390 395 400  
 Cys Val Gln Leu Ser Gln Ile Gln Ala Gln Ile Ser Ala Leu Glu Glu  
 405 410 415  
 Gln Leu Gln Gln Ile Arg Ala Glu Thr Glu Cys Gln Asn Thr Glu Tyr  
 420 425 430



Gln Gln Leu Leu Asp Ile Lys Ile Arg Leu Glu Asn Glu Ile Gln Thr  
           435                                  440                                  445  
 Tyr Arg Ser Leu Leu Glu Gly Glu Gly Ser Ser Gly Gly Gly Gly Arg  
           450                                  455                                  460  
 Gly Gly Gly Ser Phe Gly Gly Gly Tyr Gly Gly Gly Ser Ser Gly Gly  
   465                                  470                                  475                                  480  
 Gly Ser Ser Gly Gly Gly Tyr Gly Gly Gly His Gly Gly Ser Ser Gly  
                                   485                                  490                                  495  
 Gly Gly Tyr Gly Gly Gly Ser Ser Gly Gly Gly Ser Ser Gly Gly Gly  
                                   500                                  505                                  510  
 Tyr Gly Gly Gly Ser Ser Ser Gly Gly His Gly Gly Gly Ser Ser Ser  
           515                                  520                                  525  
 Gly Gly His Gly Gly Ser Ser Ser Gly Gly Tyr Gly Gly Gly Ser Ser  
           530                                  535                                  540  
 Gly Gly Gly Gly Gly Gly Tyr Gly Gly Gly Ser Ser Gly Gly Gly Ser  
   545                                  550                                  555                                  560  
 Ser Ser Gly Gly Gly Tyr Gly Gly Gly Ser Ser Ser Gly Gly His Lys  
                                   565                                  570                                  575  
 Ser Ser Ser Ser Gly Ser Val Gly Glu Ser Ser Ser Lys Gly Pro Arg  
                                   580                                  585                                  590

Tyr

<210> 11  
 <211> 458  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)..(458)  
 <223> CK13, Isoform a, Swissprot Accession NP\_705694

<400> 11

Met Ser Leu Arg Leu Gln Ser Ser Ser Ala Ser Tyr Gly Gly Gly Phe  
   1                                  5                                  10                                  15  
 Gly Gly Gly Ser Cys Gln Leu Gly Gly Gly Arg Gly Val Ser Thr Cys  
                                   20                                  25                                  30

Ser Thr Arg Phe Val Ser Gly Gly Ser Ala Gly Gly Tyr Gly Gly Gly  
 35 40 45  
 Val Ser Cys Gly Phe Gly Gly Gly Ala Gly Ser Gly Phe Gly Gly Gly  
 50 55 60  
 Tyr Gly Gly Gly Leu Gly Gly Gly Tyr Gly Gly Gly Leu Gly Gly Gly  
 65 70 75 80  
 Phe Gly Gly Gly Phe Ala Gly Gly Phe Val Asp Phe Gly Ala Cys Asp  
 85 90 95  
 Gly Gly Leu Leu Thr Gly Asn Glu Lys Ile Thr Met Gln Asn Leu Asn  
 100 105 110  
 Asp Arg Leu Ala Ser Tyr Leu Glu Lys Val Arg Ala Leu Glu Glu Ala  
 115 120 125  
 Asn Ala Asp Leu Glu Val Lys Ile Arg Asp Trp His Leu Lys Gln Ser  
 130 135 140  
 Pro Ala Ser Pro Glu Arg Asp Tyr Ser Pro Tyr Tyr Lys Thr Ile Glu  
 145 150 155 160  
 Glu Leu Arg Asp Lys Ile Leu Thr Ala Thr Ile Glu Asn Asn Arg Val  
 165 170 175  
 Ile Leu Glu Ile Asp Asn Ala Arg Leu Ala Ala Asp Asp Phe Arg Leu  
 180 185 190  
 Lys Tyr Glu Asn Glu Leu Ala Leu Arg Gln Ser Val Glu Ala Asp Ile  
 195 200 205  
 Asn Gly Leu Arg Arg Val Leu Asp Glu Leu Thr Leu Ser Lys Thr Asp  
 210 215 220  
 Leu Glu Met Gln Ile Glu Ser Leu Asn Glu Glu Leu Ala Tyr Met Lys  
 225 230 235 240  
 Lys Asn His Glu Glu Glu Met Lys Glu Phe Ser Asn Gln Val Val Gly  
 245 250 255  
 Gln Val Asn Val Glu Met Asp Ala Thr Pro Gly Ile Asp Leu Thr Arg  
 260 265 270  
 Val Leu Ala Glu Met Arg Glu Gln Tyr Glu Ala Met Ala Glu Arg Asn  
 275 280 285

Arg Arg Asp Ala Glu Glu Trp Phe His Ala Lys Ser Ala Glu Leu Asn  
290 295 300

Lys Glu Val Ser Thr Asn Thr Ala Met Ile Gln Thr Ser Lys Thr Glu  
305 310 315 320

Ile Thr Glu Leu Arg Arg Thr Leu Gln Gly Leu Glu Ile Glu Leu Gln  
325 330 335

Ser Gln Leu Ser Met Lys Ala Gly Leu Glu Asn Thr Val Ala Glu Thr  
340 345 350

Glu Cys Arg Tyr Ala Leu Gln Leu Gln Gln Ile Gln Gly Leu Ile Ser  
355 360 365

Ser Ile Glu Ala Gln Leu Ser Glu Leu Arg Ser Glu Met Glu Cys Gln  
370 375 380

Asn Gln Glu Tyr Lys Met Leu Leu Asp Ile Lys Thr Arg Leu Glu Gln  
385 390 395 400

Glu Ile Ala Thr Tyr Arg Ser Leu Leu Glu Gly Gln Asp Ala Lys Met  
405 410 415

Ile Gly Phe Pro Ser Ser Ala Gly Ser Val Ser Pro Arg Ser Thr Ser  
420 425 430

Val Thr Thr Thr Ser Ser Ala Ser Val Thr Thr Thr Ser Asn Ala Ser  
435 440 445

Gly Arg Arg Thr Ser Asp Val Arg Arg Pro  
450 455

<210> 12  
<211> 968  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)..(968)  
<223> p120, Swissprot Accession O60716

<400> 12

Met Asp Asp Ser Glu Val Glu Ser Thr Ala Ser Ile Leu Ala Ser Val  
1 5 10 15

Lys Glu Gln Glu Ala Gln Phe Glu Lys Leu Thr Arg Ala Leu Glu Glu  
20 25 30

Glu Arg Arg His Val Ser Ala Gln Leu Glu Arg Val Arg Val Ser Pro  
35 40 45

Gln Asp Ala Asn Pro Leu Met Ala Asn Gly Thr Leu Thr Arg Arg His  
50 55 60

Gln Asn Gly Arg Phe Val Gly Asp Ala Asp Leu Glu Arg Gln Lys Phe  
65 70 75 80

Ser Asp Leu Lys Leu Asn Gly Pro Gln Asp His Ser His Leu Leu Tyr  
85 90 95

Ser Thr Ile Pro Arg Met Gln Glu Pro Gly Gln Ile Val Glu Thr Tyr  
100 105 110

Thr Glu Glu Asp Pro Glu Gly Ala Met Ser Val Val Ser Val Glu Thr  
115 120 125

Ser Asp Asp Gly Thr Thr Arg Arg Thr Glu Thr Thr Val Lys Lys Val  
130 135 140

Val Lys Thr Val Thr Thr Arg Thr Val Gln Pro Val Ala Met Gly Pro  
145 150 155 160

Asp Gly Leu Pro Val Asp Ala Ser Ser Val Ser Asn Asn Tyr Ile Gln  
165 170 175

Thr Leu Gly Arg Asp Phe Arg Lys Asn Gly Asn Gly Gly Pro Gly Pro  
180 185 190

Tyr Val Gly Gln Ala Gly Thr Ala Thr Leu Pro Arg Asn Phe His Tyr  
195 200 205

Pro Pro Asp Gly Tyr Ser Arg His Tyr Glu Asp Gly Tyr Pro Gly Gly  
210 215 220

Ser Asp Asn Tyr Gly Ser Leu Ser Arg Val Thr Arg Ile Glu Glu Arg  
225 230 235 240

Tyr Arg Pro Ser Met Glu Gly Tyr Arg Ala Pro Ser Arg Gln Asp Val  
245 250 255

Tyr Gly Pro Gln Pro Gln Val Arg Val Gly Gly Ser Ser Val Asp Leu  
260 265 270

His Arg Phe His Pro Glu Pro Tyr Gly Leu Glu Asp Asp Gln Arg Ser  
275 280 285

Met Gly Tyr Asp Asp Leu Asp Tyr Gly Met Met Ser Asp Tyr Gly Thr  
 290 295 300  
 Ala Arg Arg Thr Gly Thr Pro Ser Asp Pro Arg Arg Arg Leu Arg Ser  
 305 310 315 320  
 Tyr Glu Asp Met Ile Gly Glu Glu Val Pro Ser Asp Gln Tyr Tyr Trp  
 325 330 335  
 Ala Pro Leu Ala Gln His Glu Arg Gly Ser Leu Ala Ser Leu Asp Ser  
 340 345 350  
 Leu Arg Lys Gly Gly Pro Pro Pro Pro Asn Trp Arg Gln Pro Glu Leu  
 355 360 365  
 Pro Glu Val Ile Ala Met Leu Gly Phe Arg Leu Asp Ala Val Lys Ser  
 370 375 380  
 Asn Ala Ala Ala Tyr Leu Gln His Leu Cys Tyr Arg Asn Asp Lys Val  
 385 390 395 400  
 Lys Thr Asp Val Arg Lys Leu Lys Gly Ile Pro Val Leu Val Gly Leu  
 405 410 415  
 Leu Asp His Pro Lys Lys Glu Val His Leu Gly Ala Cys Gly Ala Leu  
 420 425 430  
 Lys Asn Ile Ser Phe Gly Arg Asp Gln Asp Asn Lys Ile Ala Ile Lys  
 435 440 445  
 Asn Cys Asp Gly Val Pro Ala Leu Val Arg Leu Leu Arg Lys Ala Arg  
 450 455 460  
 Asp Met Asp Leu Thr Glu Val Ile Thr Gly Thr Leu Trp Asn Leu Ser  
 465 470 475 480  
 Ser His Asp Ser Ile Lys Met Glu Ile Val Asp His Ala Leu His Ala  
 485 490 495  
 Leu Thr Asp Glu Val Ile Ile Pro His Ser Gly Trp Glu Arg Glu Pro  
 500 505 510  
 Asn Glu Asp Cys Lys Pro Arg His Ile Glu Trp Glu Ser Val Leu Thr  
 515 520 525  
 Asn Thr Ala Gly Cys Leu Arg Asn Val Ser Ser Glu Arg Ser Glu Ala  
 530 535 540

Arg Arg Lys Leu Arg Glu Cys Asp Gly Leu Val Asp Ala Leu Ile Phe  
 545 550 555 560  
 Ile Val Gln Ala Glu Ile Gly Gln Lys Asp Ser Asp Ser Lys Leu Val  
 565 570 575  
 Glu Asn Cys Val Cys Leu Leu Arg Asn Leu Ser Tyr Gln Val His Arg  
 580 585 590  
 Glu Ile Pro Gln Ala Glu Arg Tyr Gln Glu Ala Ala Pro Asn Val Ala  
 595 600 605  
 Asn Asn Thr Gly Pro His Ala Ala Ser Cys Phe Gly Ala Lys Lys Gly  
 610 615 620  
 Lys Asp Glu Trp Phe Ser Arg Gly Lys Lys Pro Ile Glu Asp Pro Ala  
 625 630 635 640  
 Asn Asp Thr Val Asp Phe Pro Lys Arg Thr Ser Pro Ala Arg Gly Tyr  
 645 650 655  
 Glu Leu Leu Phe Gln Pro Glu Val Val Arg Ile Tyr Ile Ser Leu Leu  
 660 665 670  
 Lys Glu Ser Lys Thr Pro Ala Ile Leu Glu Ala Ser Ala Gly Ala Ile  
 675 680 685  
 Gln Asn Leu Cys Ala Gly Arg Trp Thr Tyr Gly Arg Tyr Ile Arg Ser  
 690 695 700  
 Ala Leu Arg Gln Glu Lys Ala Leu Ser Ala Ile Ala Asp Leu Leu Thr  
 705 710 715 720  
 Asn Glu His Glu Arg Val Val Lys Ala Ala Ser Gly Ala Leu Arg Asn  
 725 730 735  
 Leu Ala Val Asp Ala Arg Asn Lys Glu Leu Ile Gly Lys His Ala Ile  
 740 745 750  
 Pro Asn Leu Val Lys Asn Leu Pro Gly Gly Gln Gln Asn Ser Ser Trp  
 755 760 765  
 Asn Phe Ser Glu Asp Thr Val Ile Ser Ile Leu Asn Thr Ile Asn Glu  
 770 775 780  
 Val Ile Ala Glu Asn Leu Glu Ala Ala Lys Lys Leu Arg Glu Thr Gln  
 785 790 795 800

Gly Ile Glu Lys Leu Val Leu Ile Asn Lys Ser Gly Asn Arg Ser Glu  
805 810 815

Lys Glu Val Arg Ala Ala Ala Leu Val Leu Gln Thr Ile Trp Gly Tyr  
820 825 830

Lys Glu Leu Arg Lys Pro Leu Glu Lys Glu Gly Trp Lys Lys Ser Asp  
835 840 845

Phe Gln Val Asn Leu Asn Asn Ala Ser Arg Ser Gln Ser Ser His Ser  
850 855 860

Tyr Asp Asp Ser Thr Leu Pro Leu Ile Asp Arg Asn Gln Lys Ser Asp  
865 870 875 880

Lys Lys Pro Asp Arg Glu Glu Ile Gln Met Ser Asn Met Gly Ser Asn  
885 890 895

Thr Lys Ser Leu Asp Asn Asn Tyr Ser Thr Pro Asn Glu Arg Gly Asp  
900 905 910

His Asn Arg Thr Leu Asp Arg Ser Gly Asp Leu Gly Asp Met Glu Pro  
915 920 925

Leu Lys Gly Thr Thr Pro Leu Met Gln Asp Glu Gly Gln Glu Ser Leu  
930 935 940

Glu Glu Glu Leu Asp Val Leu Val Leu Asp Asp Glu Gly Gly Gln Val  
945 950 955 960

Ser Tyr Pro Ser Met Gln Lys Ile  
965

<210> 13  
<211> 156  
<212> PRT  
<213> Homo sapiens

<220>  
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<222> (1)..(156)  
<223> p16INK4a, Swissprot Accession P42771

<400> 13

Met Glu Pro Ala Ala Gly Ser Ser Met Glu Pro Ser Ala Asp Trp Leu  
1 5 10 15

Ala Thr Ala Ala Ala Arg Gly Arg Val Glu Glu Val Arg Ala Leu Leu  
Page 35

20                      25                      30  
 Glu Ala Gly Ala Leu Pro Asn Ala Pro Asn Ser Tyr Gly Arg Arg Pro  
           35                      40                      45  
 Ile Gln Val Met Met Met Gly Ser Ala Arg Val Ala Glu Leu Leu Leu  
       50                      55                      60  
 Leu His Gly Ala Glu Pro Asn Cys Ala Asp Pro Ala Thr Leu Thr Arg  
 65                      70                      75                      80  
 Pro Val His Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu Val Val  
                   85                      90                      95  
 Leu His Arg Ala Gly Ala Arg Leu Asp Val Arg Asp Ala Trp Gly Arg  
           100                      105                      110  
 Leu Pro Val Asp Leu Ala Glu Glu Leu Gly His Arg Asp Val Ala Arg  
       115                      120                      125  
 Tyr Leu Arg Ala Ala Ala Gly Gly Thr Arg Gly Ser Asn His Ala Arg  
 130                      135                      140  
 Ile Asp Ala Ala Glu Gly Pro Ser Asp Ile Pro Asp  
 145                      150                      155

<210> 14  
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 <222> (1)..(173)  
 <223> p14arf, Swissprot Accession Q8N726

<400> 14

Met Gly Arg Gly Arg Cys Val Gly Pro Ser Leu Gln Leu Arg Gly Gln  
 1                      5                      10                      15  
 Glu Trp Arg Cys Ser Pro Leu Val Pro Lys Gly Gly Ala Ala Ala Ala  
           20                      25                      30  
 Glu Leu Gly Pro Gly Gly Gly Glu Asn Met Val Arg Arg Phe Leu Val  
       35                      40                      45  
 Thr Leu Arg Ile Arg Arg Ala Cys Gly Pro Pro Arg Val Arg Val Phe  
       50                      55                      60



Val Val His Ile Pro Arg Leu Thr Gly Glu Trp Ala Ala Pro Gly Ala  
 65 70 75 80  
 Pro Ala Ala Val Ala Leu Val Leu Met Leu Leu Arg Ser Gln Arg Leu  
 85 90 95  
 Gly Gln Gln Pro Leu Pro Arg Arg Pro Gly His Asp Asp Gly Gln Arg  
 100 105 110  
 Pro Ser Gly Gly Ala Ala Ala Ala Pro Arg Arg Gly Ala Gln Leu Arg  
 115 120 125  
 Arg Pro Arg His Ser His Pro Thr Arg Ala Arg Arg Cys Pro Gly Gly  
 130 135 140  
 Leu Pro Gly His Ala Gly Gly Ala Ala Pro Gly Arg Gly Ala Ala Gly  
 145 150 155 160  
 Arg Ala Arg Cys Leu Gly Pro Ser Ala Arg Gly Pro Gly  
 165 170